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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/620,169	GRUSBY ET AL.	
	Examiner	Art Unit	
	Fozia M. Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *22 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/22/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

1a. Receipt of Applicants' amendment and arguments, filed on 22 December 2005 is acknowledged.

Status of Claims:

1b. Claims 1-10 have been cancelled and new claims 24-25 have been added. Thus, claims 11-25 are pending and under consideration.

1c. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. The following previous objections and rejections are withdrawn in light of Applicants' amendment filed 12/22/05.

(I) The rejection of claims 11-14, 19-23 made under 35 U.S.C. 112, second paragraph, is withdrawn, because the claims now recite method steps.

(II) The rejection of claims 11-15, 17-23 made under 35 U.S.C. 112, first paragraph for not complying with written description is withdrawn, in part. Applicants' argument that the instant specification describes how to make anti-IL-21 antibodies useful in the claimed method has been found persuasive. However, the specification fails to describe a "soluble fragment of an IL-21R". See section 4a of this office action.

Response to Applicants' arguments:

Specification:

3. The specification has been amended to correct typographical errors. No new matter has been added.

Claim Rejections under 35 U.S.C. §112:

4a. Claims 11-4, 16, 20-23 stand rejected and new claims 24-25 are rejected under 35 U.S.C. 112, first paragraph for not satisfying the written description requirements as set forth in the office action mailed on 29 July 2005.

Applicants submit that they have adequately described antagonist of IL-21R fragments and soluble receptor fragments with at least 85% identity to the extracellular portion of the 1L-21R by disclosing the sequence of the IL-21R, by identifying the extracellular domain of the IL-21R, by disclosing physical properties of antagonist IL-21R fragments, by identifying functional characteristics of such fragments, and by describing methods of making such fragments. Thus, Applicants contend that the instant disclosure, coupled with the skill and knowledge in the relevant art at the time of filing, satisfies the written description requirement of § 112, first paragraph. Applicants further argue that the instant specification discloses the full length sequence of the human IL-21 receptor, and that the IL-21R extracellular domain consists of about amino acids 20- 235. Applicants also submit that the specification discusses that the 1L-21R fragment to be used in the claimed method as a fragment which contains an IL-21 binding domain. Thus, Applicants contend that soluble IL-21R fragments useful in the claimed invention consist of regions of the extracellular domain of the IL-21R that are capable of binding an IL-21.

These arguments have been considered fully but are not deemed persuasive. Firstly, the instant specification describes the structure of the full length of the human IL-21R (SEQ ID NO:4) and proposes that the soluble fragment of an IL-21R includes an extracellular region of an IL-21 Receptor. The

specification contemplates that the extracelullar region comprises amino acids 1-235 or 20-235 of SEQ ID NO:4, (see page 4, lines 12-18 and page 5, lines 1-12). However, while the specification contemplates a soluble fragment of an IL-21R or a soluble fragment that is at least 85% identical to amino acids 20 to 235 of SEQ ID NO: 4, as recited in claim 16, that is capable of binding IL-21 receptor, it fails to describe the structure of such a soluble fragment. The specification does not describe which amino acids of amino acids 20 to 235 of SEQ ID NO: 4, can be altered without altering the desired activity of binding to IL-21 receptor. Secondly, although the level of skill in the pertinent art is quite high, however, the skilled artisan would not be able to visualize or describe what has not been conceived. Accordingly, the instant specification only describes the full length IL-21R and contemplates an extracellular domain which comprises amino acids 1-235 or 20- 235 of SEQ ID NO:4, but fails to describe an extracellular domain which comprises an amino acid sequence that is at least 85% identical to amino acids 20- 235 of SEQ ID NO:4 or a soluble fragment that is capable of binding IL-21. Regarding claims 11, 13, 24 and 25, the instant specification fails to satisfy the written description provision of 35 U.S.C. § 112, first paragraph, because although the specification discloses exemplary soluble fragments, a specific soluble fragment is not described. Accordingly, the skilled artisan would not be able to visualize the recited soluble fragment.

New Rejections:

Claim Rejections Under 35 U.S.C. § 112, first paragraph:

5a. Claims 11-18, 20-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inhibiting or reducing differentiation of a Th (Thp) cell into Th2 cell by contacting said Thp cell with an antibody that binds to IL-21R, and a method for increasing interferon gamma (IFN γ) levels in a T cell by contacting said cells with an antibody that binds to IL-21R, does not reasonably provide enablement for a method for inhibiting or reducing differentiation of a Th (Thp) cell into Th2 cell or a method for increasing interferon gamma (IFN γ) levels in a T cell, by contacting said Thp cell with a soluble fragment of an IL-21 receptor, wherein said soluble receptor comprises amino acids 20-234 of SEQ ID NO:4, and is capable of binding IL-21. The specification is also non-enabling for the therapeutic administration of an anti-IL-21 antibody, an antigen binding fragment of an anti-IL-21 antibody or a soluble fragment of an IL-21 receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, practice the invention commensurate in scope with these claims.

Claims 11, 15-18, encompass the use of "soluble fragment of an IL-21R" or "extracellular region of Il-21R), however, the specification does not disclose the use of a soluble IL-21R or the extracellular region of SEQ ID NO:4, to inhibit or reduce the differentiation of Th precursor cell into Th2 cell or to increase IFN γ levels in a T cell. The instant specification demonstrates that IL-12 inhibits IFN-gamma in Th precursor cells and that IL-21 expression was markedly increased after precursor cells were allowed to differentiate along Th2 pathway, (see examples 1-3, on pages 39-41). Thus, Applicants contemplate methods of

antagonizing IL-21 activity to increase IFN-γ levels in T cells and also to inhibit or reduce Th precursor cells differentiation into Th2 cells. While an antibody that binds to IL-21R would be expected to antagonize IL-21 activity, the art teaches that soluble receptors do not always antagonize the action of the ligand. For Example soluble receptors that bind to the ligand can either compete with the cognate receptor, thereby antagonizing the action of the ligand, or can act as binding protein to protect the ligand from degradation, thus prolonging the life of the ligand, (see Heany et al, Journal of Leukocyte Biology, Vol. 64, August 1998, pages 135-146, especially page 136, column 2 and figure 1). Regarding new claims 24-25, the instant specification does not disclose the administration of a therapeutic agent to inhibit or reduce the differentiation of a Thp cell into a Th2 or that increases IFNγ levels in a T cell. The criteria set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination. In the instant case, one skilled in the art would not be able to predict whether a soluble IL-21R or the extracellular region comprising amino acids 1-235 or 20-235 of SEQ ID NO:4, would inhibit or reduce differentiation of a Th (Thp) cell into Th2 or would increase IFN γ levels in T cells. Furthermore, it is not predictable that

antagonizing the action of IL-21 would be beneficial. IL-21 has pleitropic effects on the proliferation, differentiation and effector functions of B, T and natural killer cells. For example, IL-21 has been shown to both inhibit and promote immune responses, depending on the surrounding environment, (see Mehta et al., Immunoligcal reviews, Vol. 202, pages 84-95, 2004). Therefore, there are times where antagonizing the action of IL-21 might lead to detrimental or undesirable effects. Due to the lack of guidance as to whether a soluble IL-21R or the extracellular region comprising amino acids 1-235 or 20-235 of SEQ ID NO:4 or the extracellular region comprising amino acids at least 85% identity to amino acids 20-235 of SEQ ID NO:4, that bind to IL-21 would be antagonistic or agonistic of IL-21 activities, the complex nature of the invention, the state of the prior art which teaches that not all soluble receptors are antagonists, and the unpredictability of the effects of the administration of an antagonist of IL-21, i.e, whether the administration of an antagonist of IL-21 would be beneficial or detrimental to a subject, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Therefore, the instant specification only enables a method for inhibiting or reducing differentiation of a Th (Thp) cell into Th2 cell by contacting said Thp cell with an antibody that binds to IL-21R, and a method for increasing interferon gamma (IFN γ) levels in a T cell by contacting said cells with an antibody that binds to IL-21R, however the claims are not enabled, in so far as a soluble IL-21 receptor is concerned or the administration of a therapeutic agent wherein said

agent is an anti-IL-21R antibody or an anti-binding fragment of a n anti-IL-21R antibody or a soluble fragment of an IL-21R.

Claim Rejections - 35 U.S.C. § 112:

6. Claims 11-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6a. Claims 12 and 14 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 12 and 14 are drawn to further identifying the desired T cell, however, claims 11 and 13, from which claims 12 and 14 depend, already encompass such a limitation. Therefore, it is unclear, how claims 12 and 14 further limit the invention recited in claims 11 and 13.

6b. Claim 15 recites in line 2 "....comprises *an* extracellular region of the IL-21R...", however, it is known a receptor comprises only one extracellular region. The recitation of "an" before extracellular implies the existence of more than one extracellular region for IL-21R. Appropriate correction is required.

6c. Claims 11, 13, 24 and 25 recite ".....soluble fragment of an IL-21R", however, it is unclear which IL-21 receptor is being referred to. There is only one Known IL-21 receptor (i.e SEQ ID NO:4), therefore, the recitation of "an" before IL-21R implies the existence of more than one IL-21 receptor. Clarification is required.

Claims 16-23 are rejected under under 35 U.S.C. 112, second paragraph, so long as they depend from claims 11 and 13 for the limitations set forth above.

Conclusion:

7. No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Patent Examiner
Art Unit 1647
28 February 2006

EILEEN B. O'HARA
PRIMARY EXAMINER